



## Complete Summary

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### GUIDELINE TITLE

Vesicoureteric reflux (VUR). In: Guidelines on paediatric urology.

### BIBLIOGRAPHIC SOURCE(S)

Vesicoureteric reflux (VUR). In: Tekgul S, Riedmiller H, Gerharz E, Hoebeke P, Kocvara R, Nijman R, Radmayr C, Stein R. Guidelines on paediatric urology. Arnhem, The Netherlands: European Association of Urology, European Society for Paediatric Urology; 2008 Mar. p. 47-52. [29 references]

### GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Vesicoureteric reflux

### GUIDELINE CATEGORY

Counseling  
Diagnosis  
Evaluation  
Management  
Treatment

### CLINICAL SPECIALTY

Nephrology  
Pediatrics  
Surgery  
Urology

## **INTENDED USERS**

Physicians

## **GUIDELINE OBJECTIVE(S)**

- To outline a practical and preliminary approach to paediatric urological problems
- To increase the quality of care for children with urological problems

## **TARGET POPULATION**

Infants, children and adolescents with vesicoureteric reflux

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Diagnosis**

1. Classification: grading system for vesicoureteric reflux
2. Detailed medical/family history
3. Physical examination
4. Urinalysis, urine culture
5. Serum creatinine
6. Diagnostic imaging: ultrasound, voiding cystourethrography, radionuclide cystography using dimercaptosuccinic acid, magnetic resonance urography
7. Urodynamic studies, uroflowmetry, and/or voiding charts
8. Cystoscopy (limited recommendation)

### **Treatment/Management**

1. Medical management
  - Antibiotic prophylaxis
  - Conservative management: observation
  - Patient and parent education
2. Interventional management
  - Endoscopic subureteral injection of tissue-augmenting substances (bulking agents)
  - Laparoscopic reflux correction (considered, but not recommended as a routine procedure)
  - Open surgical correction of reflux: Lich-Gregoir; Politano-Leadbetter, Cohen and Psoas-Hitch ureteroneocystostomy; intravesical antireflux procedures for bilateral reflux
3. Treatment of underlying condition in cases of secondary vesicoureteral reflux
4. Follow-up: voiding cystourethrogram, sonography, blood pressure, urinalysis (routine radionuclide studies considered, but not recommended)

## **MAJOR OUTCOMES CONSIDERED**

- Permanent renal parenchymal damage
- Normal renal growth
- Morbidity from treatment
- Incidence of urinary tract infection (UTI)
- Incidence of refractory UTI
- Success rate of reflux repair

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Searches of Electronic Databases

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

The guidelines were based on current literature following a systematic review using MEDLINE.

### **NUMBER OF SOURCE DOCUMENTS**

Not stated

### **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

### **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

#### **Levels of Evidence**

**1a** Evidence obtained from meta-analysis of randomized trials

**1b** Evidence obtained from at least one randomized trial

**2a** Evidence obtained from at least one well-designed controlled study without randomization

**2b** Evidence obtained from at least one other type of well-designed quasi-experimental study

**3** Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports

**4** Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

## **METHODS USED TO ANALYZE THE EVIDENCE**

Systematic Review

### **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Application of a structured analysis of the literature was not possible due to a lack of well-designed studies. Whenever possible, statements have been classified in terms of level of evidence and grade of recommendation. Due to the limited availability of large randomized controlled trials – influenced also by the fact that a considerable number of treatment options relate to surgical interventions on a large spectrum of different congenital problems – this document is therefore largely a consensus document.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

### **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

- The first step in the European Association of Urology (EAU) guidelines procedure is to define the main topic.
- The second step is to establish a working group. The working groups comprise about 4-8 members, from several countries. Most of the working group members are academic urologists with a special interest in the topic. In general, general practitioners or patient representatives are not part of the working groups. A chairman leads each group. A collaborative working group consisting of members representing the European Society for Paediatric Urology (ESPU) and the EAU has gathered in an effort to produce the current update of the paediatric urology guidelines.
- The third step is to collect and evaluate the underlying evidence from the published literature.
- The fourth step is to structure and present the information. The strength of the recommendation is clearly marked in three grades (A-C), depending on the evidence source upon which the recommendation is based. Every possible effort is made to make the linkage between the level of evidence and grade of recommendation as transparent as possible.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

### **Grades of Recommendation**

- A. Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial
- B. Based on well-conducted clinical studies, but without randomized clinical studies
- C. Made despite the absence of directly applicable clinical studies of good quality

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## **METHOD OF GUIDELINE VALIDATION**

Internal Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

There is no formal external review prior to publication.

The Appraisal of Guidelines for Research and Evaluation (AGREE) instrument was used to analyse and assess a range of specific attributes contributing to the validity of a specific clinical guideline.

The AGREE instrument, to be used by two to four appraisers, was developed by the AGREE collaboration ([www.agreecollaboration.org](http://www.agreecollaboration.org)) using referenced sources for the evaluation of specific guidelines. (See the "Availability of Companion Documents" field for further methodology information).

## **RECOMMENDATIONS**

### **MAJOR RECOMMENDATIONS**

#### **Background**

The management of affected children has been directed at preventing infection and permanent renal parenchymal damage and its late complications by antibiotic prophylaxis and/or surgical correction of reflux. However, controversy remains regarding the optimal strategies for management of children with primary vesicoureteric reflux (VUR).

#### **Classification**

In 1985, the International Reflux Study Committee introduced a uniform system for the classification of VUR (see Table below). The grading system combines two earlier classifications and is based upon the extent of retrograde filling and dilatation of the ureter, the renal pelvis and the calyces on a voiding cystourethrography (VCUG). The Committee also described a standardized technique of VCUG to allow comparability of results.

**Table. Grading System for Vesicoureteric Reflux, According to the International Reflux Study Committee**

Grade I	Reflux does not reach the renal pelvis; varying degrees of ureteral dilatation
Grade II	Reflux reaches the renal pelvis; no dilatation of the collecting system; normal fornices

Grade III	Mild or moderate dilatation of the ureter, with or without kinking; moderate dilatation of the collecting system; normal or minimally deformed fornices
Grade IV	Moderate dilatation of the ureter with or without kinking; moderate dilatation of the collecting system; blunt fornices, but impressions of the papillae still visible
Grade V	Gross dilatation and kinking of the ureter, marked dilatation of the collecting system; papillary impressions no longer visible; intraparenchymal reflux

### **Diagnostic Work-up**

A basic diagnostic work-up comprises a detailed medical history (including family history), physical examination, urinalysis, urine culture and, if renal function needs to be assessed, serum creatinine level. Diagnostic imaging for VUR encompasses both radiological and sonographic modalities. Radiological modalities comprise VCUG, the most widespread method for examination of reflux, and radionuclide cystography (RNC).

In RNC, radiation exposure is significantly lower than in VCUG with continuous fluoroscopy, but the anatomical details depicted are much more inferior. With the introduction of pulsed fluoroscopy, the radiation exposure of VCUG could be markedly reduced. The use of VCUG allows the grade of reflux to be determined (in a single or duplicated kidney) and the assessment of bladder and ureteral configuration. Moreover, VCUG is the study of choice for imaging the urethra. The sonographic diagnosis of VUR with intravesical administration of an ultrasound (US) contrast agent (voiding urosonography [VUS]) is mostly used as the primary reflux examination modality in girls and during follow-up.

In complex cases, magnetic resonance urography may be required for evaluation of the upper urinary tract.

Dimercaptosuccinic acid (DMSA) is the best nuclear agent for visualizing cortical tissue, evaluating renal parenchyma, and documenting the presence of renal scars. Children with normal DMSA during an acute urinary tract infection (UTI) have a low risk of renal damage. Children with normal follow-up DMSA and low-grade VUR have more frequent spontaneous resolution of VUR.

In the case of incontinence or residual urine, urodynamic studies can be performed to reveal functional abnormalities of the lower urinary tract. Such testing is most important in patients in whom secondary reflux is suspected, such as patients with spina bifida or boys whose VCUG is suggestive of residual posterior urethral valves. Yet, in most cases of non-neurogenic voiding dysfunction, diagnosis and follow-up can be limited to non-invasive tests (voiding charts, US, uroflowmetry). In the few remaining children with inconclusive findings and who are refractory to treatment, urodynamic tests are necessary. Appropriate management of voiding dysfunction will often result in the resolution of reflux.

In the past, cystoscopy was considered to be essential for the assessment of VUR. The position and shape of the ureteral orifices were thought to correlate with the grade and prognosis. Subsequent data have demonstrated that cystoscopic

observations do not contribute significantly to the outcome of management. Cystoscopy may be performed at the time of open surgery to identify additional anatomical abnormalities, such as ureteral duplication and ureteral ectopia.

**Treatment**

Early diagnosis and vigilant monitoring are the cornerstones of treatment (see the table below). The ultimate objective of treatment is to allow normal renal growth and to prevent permanent renal parenchymal damage and its late complications (reflux nephropathy, see the original guideline document). There is no single therapeutic strategy for all clinical settings of VUR.

Therapeutic options comprise conservative (medical) management, including antibiotic prophylaxis, and interventional approaches (i.e., endoscopic subureteral injection, laparoscopic or open surgical correction of reflux), in isolation or combined.

The individual choice of management is based on the presence of renal scars, the clinical course, grade of reflux, ipsilateral renal function, bilaterality, bladder capacity and function, associated anomalies of the urinary tract, age, compliance and parental preference.

Surgical correction is warranted in recurrent febrile infections despite antibiotic prophylaxis (breakthrough infections), medical non-compliance, and new scars and in the presence of associated malformations (e.g., duplex systems, Hutch diverticulum, ectopic ureter).

In secondary VUR, the objective of management is treatment of the underlying condition. If VUR persists after successful therapy of the underlying condition, further management depends on the individual clinical setting.

**Table. Treatment of Reflux**

<b>Patient's Age</b>	<b>Grade of Reflux/Gender</b>	<b>Management</b>
<1 year		Conservative
1-5 year(s)	Grade I-III	Conservative
	Grade IV-V	Surgical correction
>5 years	Boys	Indication for surgery is rare
	Girls	Surgical correction

**Conservative Approach**

The rationale for conservative management is the observation that VUR can resolve spontaneously with time, mostly in young patients with low-grade reflux (81% and 48% in VUR grades I-II and III-V, respectively). The objective of conservative therapy is prevention of febrile UTI.

Education and consistent follow-up of the patient and parent, high fluid intake, regular and complete emptying of the bladder (if necessary with double micturition) and low-dose antibiotic prophylaxis are key aspects of conservative management. In boys with low-grade VUR, circumcision may be advised.

Conservative management should be dismissed in favour of surgical intervention in all cases of febrile breakthrough infections, as well as in girls in whom VUR has persisted up to an age at which spontaneous resolution can no longer be expected. In boys 5 years and older antibiotic prophylaxis may be stopped, and indications for surgical reflux correction are rare.

## **Interventional Therapy**

### *Open Surgery*

Various intra- and extra-vesical techniques have been described for the surgical correction of reflux. Although different methods have specific advantages and complications, they all share the basic principle of lengthening the intramural part of the ureter by submucosal embedding of the ureter. All techniques have been shown to be safe with a low rate of complications and excellent success rates (92%-98%). Currently, the most popular procedures are the Lich-Gregoir, Politano-Leadbetter, Cohen and Psoas-Hitch ureteroneocystostomy.

Surgery in early infancy carries a high risk of severely damaging bladder function. If an extravesical procedure is planned, cystoscopy should be performed preoperatively to assess the bladder mucosa and position and configuration of the ureteric orifices. In bilateral reflux, intravesical antireflux procedures may be considered, as simultaneous bilateral extravesical reflux repair carries an increased risk of temporary postoperative urine retention.

### *Laparoscopic Reflux Correction*

In a small number of children, VUR has been corrected laparoscopically. Although success rates are similar to open surgery, laparoscopic reflux correction takes significantly longer and therefore has no obvious advantages. At present, a laparoscopic approach cannot be recommended as a routine procedure.

### *Endoscopic Therapy*

Although still mainly experimental, endoscopic treatment of VUR offers the advantage of enabling treatment of the underlying anatomical defect while avoiding the morbidity of open surgery. With the availability of biodegradable substances, endoscopic subureteral injection of tissue-augmenting substances (bulking agents) have become an alternative to long-term antibiotic prophylaxis and surgical intervention in the treatment of VUR in children. Although there is not yet a prospective trial proving that endoscopic therapy is equally effective as the conservative management, endoscopic therapy is currently being used as the initial treatment of reflux in some centres. A sound clinical validation of its effectiveness is currently hampered by the lack of methodologically appropriate studies.

## Follow-up

Follow-up after surgical correction of VUR is a controversial issue. In a recent update of the International Reflux Study, the authors published the results of urography at 10 years after either medical or surgical treatment of VUR. They concluded that with careful management, only a small proportion of children with severe reflux developed new scars and then rarely after the first 5-year follow-up period, and that there was no difference between children treated medically or surgically. Routine radionuclide studies are therefore not recommended.

As post-operative VCUG does not allow identification of children at risk of developing febrile UTI, this investigation is optional. Although VCUG may not be necessary in clinically asymptomatic cases after open surgery, it is mandatory following endoscopic treatment.

Obstruction of the upper urinary tract is ruled out by sonography at discharge and 3 months postoperatively. The follow-up protocol should include blood pressure measurement and urinalysis.

## CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Appropriate diagnosis, treatment, and management of vesicoureteric reflux in children
- Prevention of urinary tract infection
- Prevention of permanent renal parenchymal damage and its late complications
- Normal renal growth

### POTENTIAL HARMS

- Radiation exposure from diagnostic imaging procedures
- Surgery in early infancy carries a high risk of severely damaging bladder function.
- Simultaneous bilateral extravesical reflux repair carries an increased risk of temporary postoperative urine retention.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

The purpose of these texts is not to be proscriptive in the way a clinician should treat a patient but rather to provide access to the best contemporaneous consensus view on the most appropriate management currently available. European Association of Urology (EAU) guidelines are not meant to be legal documents but are produced with the ultimate aim to help urologists with their day-to-day practice.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

The European Association of Urology (EAU) Guidelines long version (containing all 19 guidelines) is reprinted annually in one book. Each text is dated. This means that if the latest edition of the book is read, one will know that this is the most updated version available. The same text is also made available on a CD (with hyperlinks to PubMed for most references) and posted on the EAU websites Uroweb and Urosource ([www.uroweb.org/professional-resources/guidelines/](http://www.uroweb.org/professional-resources/guidelines/) & <http://www.urosource.com/diseases/>).

Condensed pocket versions, containing mainly flow-charts and summaries, are also printed annually. All these publications are distributed free of charge to all (more than 10,000) members of the Association. Abridged versions of the guidelines are published in European Urology as original papers. Furthermore, many important websites list links to the relevant EAU guidelines sections on the association websites and all, or individual, guidelines have been translated to some 15 languages.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Vesicoureteric reflux (VUR). In: Tekgul S, Riedmiller H, Gerharz E, Hoebeke P, Kocvara R, Nijman R, Radmayr C, Stein R. Guidelines on paediatric urology. Arnhem, The Netherlands: European Association of Urology, European Society for Paediatric Urology; 2008 Mar. p. 47-52. [29 references]

## **ADAPTATION**

Not applicable: The guideline was not adapted from another source.

## **DATE RELEASED**

2008 Mar

## **GUIDELINE DEVELOPER(S)**

European Association of Urology - Medical Specialty Society  
European Society for Paediatric Urology - Medical Specialty Society

## **SOURCE(S) OF FUNDING**

European Association of Urology

## **GUIDELINE COMMITTEE**

Not stated

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

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## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

All members of the working group submit a conflict of interest form. The information is kept on file in the European Association of Urology (EAU) Central Office database. This guidelines document was developed with the financial support of the EAU. No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative assistance, travel, and meeting expenses. No honoraria or other reimbursements have been provided.

## **GUIDELINE STATUS**

This is the current release of the guideline.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available in Portable Document Format (PDF) from the [European Association of Urology Web site](#).

Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803, AA ARNHEM, The Netherlands.

#### **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

- EAU guidelines office template. Arnhem, The Netherlands: European Association of Urology (EAU); 2007. 4 p.
- The European Association of Urology (EAU) guidelines methodology: a critical evaluation. Arnhem, The Netherlands: European Association of Urology (EAU); 18 p.

Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803, AA ARNHEM, The Netherlands.

#### **PATIENT RESOURCES**

None available

#### **NGC STATUS**

This NGC summary was completed by ECRI Institute on November 17, 2008. The information was verified by the guideline developer on December 19, 2008.

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